STEPHEN S. RABINOWITZ
stephen.rabinowitz@hugheshubbard.com
JAMES W. DABNEY (*Pro Hac Vice)*
james.dabney@hugheshubbard.com
PATRICE P. JEAN (*Pro Hac Vice)*
patrice.jean@hugheshubbard.com
WANDA D. FRENCH-BROWN (*Pro Hac Vice*)
wanda.french-brown@hugheshubbard.com
MITCHELL EPNER (*Pro Hac Vice*)
mitchell.epner@hugheshubbard.com
DAVID E. LANSKY (*Pro Hac Vice*)
david.lansky@hugheshubbard.com
HUGHES HUBBARD & REED LLP
One Battery Park Plaza
New York, NY 10004
Telephone: 212-837-6000
Facsimile: 212-299-6807

JOSHUA H. LERNER (SBN 220755)
jlerner@durietangri.com
LAURA E. MILLER (SBN 271713)
lmiller@durietangri.com
Durie Tangri LLP
217 Leidesdorff Street
San Francisco, CA 94111
Telephone: 415-362-6666
Facsimile: 415-236-6300

[Counsel continued overleaf]

Attorneys for Defendant
MERCK & CO., INC. and Defendants and Counterclaimants
MERCK SHARP & DOHME CORP. and ISIS PHARMACEUTICALS, INC.

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

GILEAD SCIENCES, INC.,

Plaintiff and Counterdefendant,

v.

MERCK & CO., INC. (Defendant only), MERCK SHARP & DOHME CORP., and ISIS PHARMACEUTICALS, INC.

Defendants and Counterclaimants.

Case No. 5:13-cv-04057-BLF

DEFENDANTS' OPPOSITION TO GILEAD'S MOTION FOR SUMMARY JUDGMENT OF INVALIDITY

Date: December 10, 2015
Time: 9:00 a.m.
Ctrm: 3, 5th Floor
Judge: Honorable Beth Labson Freeman

RANDY C. EISENSMITH (Pro Hac Vice)
randy.eisensmith@friedfrank.com
NAZ E. WEHRLI (Pro Hac Vice)
naz.wehrli@friedfrank.com
FRIED, FRANK, HARRIS, SHRIVER & JACOBSON LLP
ONE NEW YORK PLAZA
NEW YORK, NY 10004
Telephone: 212-859-8000
Facsimile: 212-859-4000

TABLE OF CONTENTS

TABLE OF AUTHORITIES

PAGE(S)

Cases

Statutes

Rules

Defendants Merck & Co, Inc., Merck Sharp & Dohme Corp. and Isis Pharmaceuticals, Inc. (collectively, "Merck") respectfully submit this Memorandum of Law in Opposition to the Motion for Summary Judgment of Invalidity (ECF 164-3) ("Motion") in which Gilead Sciences, Inc. ("Gilead") contends that claims 1 and 2 (the "Asserted Claims") of U.S. Patent No. 7,105,499 (the "'499 Patent") and claims 1-3, 5, 7 and 9-11 (the "Asserted Claims") of U.S. Patent No. 8,481,712 (the "'712 Patent") (collectively, the "Patents-in Suit") are invalid for lack of practical utility. For the reasons set forth below, Gilead's Motion should be denied in its entirety.

I. INTRODUCTION

Gilead begins its brief by noting that patent law is grounded in the fundamental bargain that the inventor is granted the exclusionary monopoly of a patent right in exchange for disclosing a useful invention to the public. *See* ECF 164-3 at 1. One reason why patents are valuable to the public is that "such public disclosures will stimulate others to add to the sum of human knowledge through the creation of other inventions utilizing the lessons learned by the patentee." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 621 (Fed. Cir. 2000) (en banc) (Linn, J., concurring in part and dissenting in part), *vacated*, 535 U.S. 722 (2002). In July, 2002, Drs. Carroll, Olsen, MacCoss, Bhat, Cook, Eldrup and Prakash ("Carroll et al.") published the specification of the '499 Patent, which Pharmasset scientists admit [redacted]. A jury is entitled to conclude that Gilead benefited from the public disclosure of Merck's invention. Now, having copied Merck's invention, Gilead has the temerity to assert that one of skill in the art would not have believed that the very specification Gilead copied established a credible utility. In other words, having copied the invention, Gilead now insists that no-one would have believed the invention was worth copying.

Gilead's motion for summary judgment falls far short of the weighty burden it must meet. Gilead, as the party seeking to invalidate duly issued and presumptively valid patents, bears the burden of proving invalidity by clear and convincing evidence. Merck, as the party resisting summary judgment, is entitled to have all factual disputes decided (and all reasonable inferences made) in its favor. In order to prove a lack of "practical utility," given that the Patents-in-Suit disclose that the inventions are useful for (a) inhibiting the HCV NS5B polymerase and (b) treatment of HCV infection, Gilead must prove by clear and convincing evidence that any person of ordinary skill in the art who, on January 18, 2002, read

these allegations of practical utility, would consider them as untrustworthy and incredible as a claim to have invented a perpetual motion machine, or cold fusion.

Gilead does not acknowledge, and does not meet, this burden. It has misstated the law and misrepresented the facts. Gilead's Motion must be denied for least five independent reasons:

First, far from it being implausible that nucleoside analogs were useful to (a) inhibit replication of the HCV NS5B polymerase or (b) to treat HCV infection, it was well known by January 2002 that nucleoside analogs were the "cornerstone" of modern anti-viral treatments. Dr. Raymond Schinazi — the founder of Pharmasset — had published in 1999 that "2'-fluoronucleosides are biologically active molecules which are useful in the treatment of . . . hepatitis C." By January 2002, at least seventeen nucleoside analogs had been approved by the Food and Drug Administration ("FDA") to treat a wide-range of viral infections, including HCV. Thus, given the state of the art, the specification did not need to include any data whatsoever to establish the asserted utility. At the very least, this evidence raises a factual dispute that precludes summary judgment of invalidity.

Second, Gilead literally has offered no evidence to gainsay the usefulness of the compounds of the '712 patent to inhibit the HCV NS5B polymerase in a cell-free assay. To the contrary, Gilead's own expert admitted at deposition that the NS5B polymerase inhibitors have utility. This admission precludes summary judgment of invalidity (and would support summary judgment that the '712 Patent is ***not*** invalid for lack of practical utility).

Third, although corroborating data was not required to be included in the Patents-in-Suit to support the asserted utility, ample data were in fact provided in the specification, which described assays that were performed on exemplified compounds and summarized the results obtained. Merck's experts provided detailed testimony on this topic and explained how the results obtained with the exemplified compounds support the utility of the claimed compounds and methods. At a minimum, this evidence raises a factual dispute that precludes summary judgment.

Fourth, even if data were required (and it is not) and even if the specifications had not provided data (though they do), Merck can rely on post-filing data to support the asserted utility, including data generated by others. Indeed, Merck's proof that Gilead infringes the Patents-in-Suit, by itself, requires denial of Gilead's motion for summary judgment. Gilead stood on Merck's shoulders when it developed

sofosbuvir, and the evidence shows that Gilead's sofosbuvir products utilize the invention claimed in the Patents-in-Suit. The law is clear that a finding of infringement constitutes evidence of practical utility. Thus, evidence of infringement at least raises a factual dispute that precludes summary judgment.

Fifth, the scientific data concerning sofosbuvir and the enormous commercial success of Gilead's sofosbuvir products, Sovaldi and Harvoni (the "Accused Products"), selling [redacted] dollars of product at a gross margin of over [redacted]%, are further evidence of utility and provide a separate and sufficient basis for denying Gilead's motion.

For all of the foregoing reasons, and the reasons set forth in detail below, Merck respectfully submits that this Court must deny Gilead's motion for summary judgment of invalidity.

A. STATEMENT OF ISSUES TO BE DECIDED

Whether, given that the specification of the '712 Patent discloses that the 5'-triphosphate nucleoside compounds of the invention are useful as inhibitors of the Hepatitis C virus (HCV) NS5B polymerase, a reasonable jury could find that Gilead has not met its burden to prove by clear and convincing evidence that the '712 Patent specification fails to disclose a practical utility for those compounds, namely: inhibition of the HCV NS5B polymerase.

Whether, given that the specifications of the '499 and '712 Patents[1] disclose that the nucleoside compounds of the invention are useful to treat HCV infection, a reasonable jury could find that Gilead has not met its burden to prove by clear and convincing evidence that the '499 and '712 Patent specifications fail to disclose a practical utility for those compounds, namely: treatment of HCV infection.

II. COUNTERSTATEMENT OF THE RELEVANT FACTS

A. Pharmasset Based Its Work on the Disclosure of the '499 Patent

Gilead's contention that the Patents-in-Suit fail to disclose a practical utility is debunked by the undisputed fact that Pharmasset (later acquired by Gilead) grounded its HCV nucleoside research on the disclosure of the published PCT Application that issued as the '499 Patent. It is undisputed that the disclosure of the '499 Patent was published as a PCT Application on July 25, 2002, under PCT

[1] It is undisputed that the specifications of the '499 and '712 Patents contain the same substantive disclosures with regard to the issues raised by Gilead's Motion. *See* ECF 164-3 at 6 n. 4.

Publication No. WO02/057425 (the "Merck '499 Publication"). ECF 1-1 (cover page). It is further undisputed that [redacted] Declaration of Mitchell Epner in Support of Defendants' Opposition to Gilead's Motion for Summary Judgment of Invalidity, Exhibit ("Ex.") 1 at GILEAD05003447-48.[2]

Pharmasset documents contemporaneously recorded Pharmasset's leading scientists (including Michael Otto (Chief Scientific Officer) and Kyoichi A. Watanabe (then-Chief Chemist)) describing the [redacted]

Ex. 2 at GILEAD00218571. Likewise, Pharamasset's January 17, 2003 Chemistry Minutes capture [redacted]

Ex. 3 at GILEAD00219778-79 (emphasis added).

At Pharmasset, copying from Merck's patent disclosure was so pervasive [redacted]

[2] Exhibits to the Epner Declaration are identified in this brief as "Ex. __"; exhibits to other documents are identified with the title of the document and the exhibit number.

[redacted]

ECF 159-42 at 154:23-155:11. Elsewhere, Pharmasset's Chemistry Meeting Notes record Dr. Otto instructing Pharmasset's scientists, [redacted] Ex. 1 at GILEAD05003447.

Moreover, the contemporaneous record demonstrates that Pharmasset's scientists understood that

[redacted]

Ex. 4 at GILEAD02363309 (emphasis in original).

These undisputed facts debunk Gilead's fallacious contention that Merck in some way based its invention on work performed at Pharmasset. The due diligence discussions between Pharmasset and Merck that Gilead cites occurred in 2004, years after (a) Merck had filed and published the PCT Application that issued as the '499 Patent; and (b) Pharmasset had patterned its HCV nucleoside development efforts on the disclosures of the Merck PCT Application. Pharmasset's scientists stood on Merck's shoulders in developing sofosbuvir and not the other way round, as suggested in Gilead's Motion.

[3] Dr. Otto admitted at his deposition that he, Michael J. Otto, was referred to as "MJO" in this document. ECF 159-42 at 211:3-10.

B. The Disclosure of the '499 and '712 Specifications

The '499 Patent issued from an International (PCT) Application filed on January 18, 2002. ECF 1-1 (cover page); Declaration of Stephen S. Rabinowitz in Support of Defendants' Opposition to Gilead's Motion for Summary Judgment ("Rabinowitz Decl."), Exs. 1 (application as filed) & 3 (prosecution history). The '712 Patent issued from a non-provisional U.S. application filed on January 18, 2002, through a series of divisional and continuation applications. ECF 1-2 (cover page); Rabinowitz Decl., Exs. 2 (providing application as filed) & 4 (prosecution history).

The Patents-in Suit disclose inventions that arose from a collaboration between Dr. Steven Carroll and his colleagues at Merck & Co., Inc. and Isis Pharmaceuticals, Inc., aimed at providing: (i) "nucleoside compounds and certain derivatives thereof which are **useful as** . . . **inhibitors of HCV NS5B polymerase**" and (ii) "nucleoside compounds and certain derivatives which are **useful in** . . . **the treatment of HCV infection**." ECF 1-1 2:41-45, 50-53; ECF 1-2 2:51-55, 60-63 (emphasis added). The Patents-in-Suit define the compounds of the invention by means of structural formulas in the specification, *see, e.g.*, ECF 1-1 13:1-14:49; ECF 1-2 13:15-14:67, and illustrate the invention by 154 working examples, *see* ECF 1-1cols. 40-131, ECF 1-2 cols. 41-137, in addition to other teachings in the specification. The Patents-in Suit provide results from two biological assays for efficacy: inhibition of HCV NS5B polymerase and inhibition of HCV RNA replication. *See* ECF 1-1 132:1-133:26; ECF 1-2 137:63-139:19. With respect to inhibition of HCV NS5B polymerase, the specifications report the following results: "Representative compounds tested in the HCV NS5B polymerase assay exhibited IC_{50}'s less than 100 micromolar." ECF 1-1 132:56-57; ECF 1-2 138:49-50. With respect to the inhibition of HCV RNA replication, the specifications report the following results: "Representative compounds tested in the replication assay exhibited EC_{50}'s less than 100 micromolar." ECF 1-1 133:22-23; ECF 1-2 139:15-16.

As Dr. James D. Wuest, Professor of Chemistry at the University of Montreal, explained in his expert report, the specifications of the Patents-in-Suit showed that Carroll et al. engaged in a "major endeavor requiring a significant amount of time" regarding nucleosides and their corresponding triphosphates. Rebuttal Report of Dr. James D. Wuest (Epner Decl., Ex. 51) ¶ 82. Using the HCV RNA Replication ("replicon") assay, Carroll et al. identified a set of compounds with "**key structural features**

related to their use in treating RNA viral infections such as **HCV infection**" by virtue of "**a selective ability to inhibit** RNA viral polymerases, and in particular **the HCV NS5B polymerase**." *Id*. ¶¶ 95, 107, 110 (emphasis added). *See id*. ¶ 109 (depicting those key structural features in structure 1).

> A person of ordinary skill would therefore have recognized that a key aspect of the inventions set out in the patents-in-suit is the following discovery: Natural ribonucleosides can be modified by making the structural alterations shown in structure 1 (including the addition of a methyl group or a related small substituent at the 2' position) without preventing the unnatural compounds from acting as imposters that can be phosphorylated to give triphosphates **that inhibit HCV NS5B polymerase and viral replication**.

Id. ¶ 113 (emphasis added).

The specifications show that: (a) Carroll et al. "had engaged in a systematic, time consuming effort to discover compounds with the potential to inhibit viral RNA replication and to be useful as agents for treating viral infections [including] conceiving and preparing a large number of compounds, many made for the first time, as well as testing these compounds using pertinent biological assays," *id*. ¶ 115; (b) there was "a solid foundation of evidence that led the inventors to conclude that compounds of the particular subgenus set out in Claims 1 and 2 [of the '499 Patent] can inhibit HCV NS5B polymerase and HCV RNA replication," *id*. ¶ 146; and (c) Carroll et al. "provided a large body of data in support of their claims" *Id*. ¶75. A reasonable jury is entitled to credit Dr. Wuest's expert testimony and conclude that Carroll et al. identified the "key structural features" that define nucleoside analogs that are useful for (a) inhibiting the HCV NS5N polymerase and (b) treating HCV infections.

C. Prior Art Antiviral Nucleoside Analogs

As of January 18, 2002, it was well established in the art that nucleoside analogs could be highly effective—the "cornerstone"—for treatment of a wide variety of viral infections. As a review article published in August, 2001 explained:

> Nucleoside analogues have been the cornerstone of antiviral therapy over the past 30 years. Currently, 6 out of the 15 drugs available for the treatment of AIDS . . . belong to this category . . . . Ribavirin . . . a nucleoside analogue . . . is the only approved drug for treatment of hepatitis C (HCV) infection in combination with interferon-α.

(Gumina et al.) Ex. 6 at 9.

Gilead is flatly wrong when it contends: "[A]s of January 2002, the usefulness of a nucleoside

with fluorine substituted at the 2' position . . . would have been particularly uncertain . . . ." ECF 164-3 at 10. On the contrary, Dr. Raymond Schinazi—the founder of Pharmasset—announced in his patent application, published on September 2, 1999 that "2'-Fluoronucleoside compounds are disclosed which are useful in treatment of . . . hepatitis C infection . . . ." (Schinazi et al.) Ex. 52 (Abstract). The U.S. Patent and Trademark Office subsequently issued this patent with HCV treatment claims. As Dr. Schinazi explained:

> The 2'-fluoronucleosides are biologically active molecules which are **useful in the treatment of** hepatitis B, **hepatitis C** or HIV. . . . One can easily determine the spectrum of activity by evaluating the compound in the assays described herein or with another confirmatory assay.

Id. at 11:9-13 (emphasis added); *see also id*. at 79:14-25 ("Compounds can exhibit anti-hepatitis C activity by inhibiting HCV polymerase . . . ."; identifying "HCV polymerase assay[s]" for "evaluat[ing] the activity of the compounds disclosed herein" against HCV). In addition, a 1990 publication by scientists at Roche reported on the "synthesis and biological properties of some monofluoro and difluoro analogues of dideoxynucleotides," (Martin et al.) Ex. 50 at 2138, and disclosed that a "**2'-fluoro analogue**" called "compound 35" had "**antiviral activity** with an IC_{50} value of 10 µM [micromolar]" and was "**not toxic** to the host lymphoblastoid cells at a concentration of 100 µM." *Id*. at 2139 (emphasis added).

By January 18, 2002, the FDA had approved many nucleoside analogs as safe and effective for the treatment of large number of viral infections, including the seventeen (17) nucleoside analogs identified in the table below for the treatment of nine (9) viral infections, including HCV:

Name	Approved Therapeutic Use(s)	Evidence
Idoxuridine	Herpes simplex virus	Exs. 7, 8
Vidarabine	Herpes simplex virus-1	Exs. 9, 10
Trifluridine	Herpes simplex virus-1	Exs. 11, 12
Acyclovir	Herpes simplex virus-1, Herpes simplex virius-2, Varicella zoster virus	Exs. 13, 14
Ribavirin	Hepatitis C virus (HCV)	Exs. 15, 16
Zidovudine	Human immunodeficiency virus (HIV)	Exs. 17, 18
Ganciclovir	Cytomegalovirus	Exs. 19, 20
Didanosine	Human immunodeficiency virus (HIV)	Exs. 21, 22

Name	Approved Therapeutic Use(s)	Evidence
Zalcitabine	Human immunodeficiency virus (HIV)	Exs. 23, 24
Stavudine	Human immunodeficiency virus (HIV)	Exs. 25, 26
Famciclovir	Herpes zoster virus	Exs. 27, 28
Valacyclovir	Herpes simplex virus, Herpes zoster virus, Herpes labialis virus	Exs. 29, 30
Lamivudine	Human immunodeficiency virus (HIV), Hepatitis B virus (HBV)	Exs. 33, 34
Penciclovir	Herpes labialis virus	Exs. 31, 32
Abacavir	Human immunodeficiency virus (HIV)	Exs. 38, 39
Valganciclovir	Cytomegalovirus	Exs. 40, 41
Tenofovir	Human immunodeficiency virus (HIV)	Exs. 42, 43

III. LEGAL STANDARDS

A. The Presumption of Validity

35 U.S.C. § 282 provides, in relevant part:

> A patent shall be presumed valid. Each claim of a patent . . . shall be presumed valid independently of the validity of other claims . . . The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.

Section 282 places the burden on Gilead to prove invalidity by clear and convincing evidence. *Microsoft Corp. v. i4i Limited P'ship*, 131 S. Ct. 2238, 2242 (2011).

B. Summary Judgment

Summary judgment is appropriate only where there is no genuine issue as to any material fact and the movant is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(a); *Nike Inc. v. Wolverine World Wide, Inc.*, 43 F.3d 644, 646 (Fed. Cir. 1994). The court must make all reasonable inferences and assess the evidence in the light most favorable to the non-moving party. *Lemire v. Cal. Dept. of Corrections and Rehabilitation*, 726 F.3d 1062, 1084 (9th Cir. 2013). The moving party bears the initial burden of demonstrating the absence of a genuine dispute as to any material fact. *Celotex Corp. v. Catrett*, 477 U.S. 317, 323 (1986). A genuine dispute exists if the issue of fact could reasonably be resolved in favor of either party. The dispute is "material" if it could affect the outcome of the suit under governing law. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248-49 (1986). The burden then shifts to the non-moving

party to "go beyond the pleadings and by her own affidavits, or by the depositions, answers to interrogatories, and admissions on file, designate specific facts showing that there is a genuine issue for trial." *Celotex*, 477 U.S. at 324 (internal quotation marks omitted).

In ruling on a motion for summary judgment, the judge must view the evidence through the prism of the substantive evidentiary burden. *Anderson*, 477 U.S. at 254. Where a "clear and convincing" evidence requirement applies (as it does to Gilead's Motion), "the trial judge's summary judgment inquiry as to whether a genuine issue exists will be whether the evidence presented is such that a jury applying that evidentiary standard could reasonably find either for the plaintiff or the defendant." *Id*. at 255. To make out a prima facie case, Gilead must present "clear and convincing" evidence that the challenged claims lack a supporting utility. If Gilead fails to make such a showing, or if Merck presents evidence on which the jury could reasonably find that the "clear and convincing" standard is not met, summary judgment must be denied. *Id*. at 252.

C. Utility

The utility requirement is set forth in section 101 of the Patent Statute, as follows:

> Whoever invents or discovers any new and **useful** process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

35 U.S.C. § 101 (emphasis added). Utility is a fact question. *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 956 (Fed. Cir. 1983). The utility requirement is closely related to the enablement requirement, set forth in the section 112 of the Patent Statute, as follows:

> The specification shall contain a written description of the invention, and of the manner and process of making and **using** it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . . .

35 U.S.C. § 112, first paragraph (emphasis added).

"If a patent claim fails to meet the utility requirement because it is not useful or operative, then it also fails to meet the how-t-use aspect of the enablement requirement. *Process Control Corp. v. Hydreclaim Corp.*, 190 F.3d 1350, 1358 (Fed. Cir. 1999); *accord In re Brana*, 51 F.3d 1560, 1564 n.12 (Fed. Cir. 1995) ("[A]bsence of utility can be the basis of a rejection under both 35 U.S.C. § 101 and 35

U.S.C. § 112 ¶ 1."). "Invalidity for lack of enablement is a conclusion of law and must be supported by facts proved by clear and convincing evidence." *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990).

The Supreme Court's decision in *Brenner v. Manson* provides "broad guidelines which are helpful in ascertaining what constitutes practical utility for compounds having a pharmacological effect." *Cross v. Iizuka*, 753 F.2d 1040, 1046 (Fed. Cir. 1985) (citing *Brenner v. Manson*, 383 U.S. 519 (1966)). In applying *Brenner*, the Federal Circuit has explained:

> Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility.

Nelson v. Bowler, 626 F.2d 853, 856 (Fed. Cir. 1980) (practical utility was established by "rough screens" that evidence some pharmacological activity "even though they may not establish a specific therapeutic use" because "a rigorous correlation is not necessary where the test for pharmacological activity is reasonably indicative of the desired response."); *accord Cross*, 753 F.2d at 1050 ("[Adequate proof of any pharmacological activity constitutes a showing of practical utility.") (applying *Nelson*, 626 F.2d at 856).

In *Brana*, the Federal Circuit reversed the examiner's rejection under 35 U.S.C. § 112 for lack of utility, and held that utility was sufficiently disclosed where the specification stated that the claimed compounds have "a better action and a better action spectrum as antitumor substances" than known compounds. *Brana*, 51 F.3d at 1565; *see* U.S. Patent No. 5,552,544 (Ex. 44) at 1:35-36. As the Court explained:

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Brana, 51 F.3d at 1566 (holding that the PTO had not satisfied its "initial burden of challenging a

presumptively correct assertion of utility in the disclosure" so as to "shift [the burden] to the applicant to provide rebuttal evidence" in support of the asserted utility) (quoting *In re Marzocchi*, 439 F.2d 220, 223 (CCPA 1971)). As the Federal Circuit and its predecessor court have emphasized:

> [I]n the usual case where the mode of operation alleged can be readily understood and conforms to the known laws of physics and chemistry, operativeness is not questioned and no further evidence is required.

In re Chilowski, 229 F.2d 457, 462 (CCPA 1956) (explaining that operativeness may be questioned "if the alleged operation seems clearly to conflict with a recognized scientific principle, as for example where an applicant purports to have discovered a machine producing perpetual motion" or when the claimed device is "of such a nature that it could not be tested by any known scientific principles."); *accord Brana*, 51 F.3d at 1566 n.17 (quoting and applying *Chilowski*).

An assertion of utility in the specification must be accepted unless there is "reason to doubt the objective truth of the statements contained in the written description." *In re Cortright*, 165 F.3d 1353, 1357 (Fed. Cir. 1999). Such a "reason to doubt" exists only where the asserted utility "suggest[s] an inherently unbelievable undertaking or involve[s] implausible scientific principles." *Id*. (alterations in original) (finding that the claimed "method for the restoration of hair growth" was not "inherently unbelievable" because other treatments for baldness "have gained acceptance" and reversing rejection under §§ 101 and 112 for lack of utility and failure to enable).

To the extent data supporting utility is required, the Patents-in-Suit provide it. In *Brana*, as here, the invention concerned a genus of novel compounds, defined by a structural formula. Ex. 44 at 1:15-36; 4:24-46. The **entirety** of the evidence of utility provided in the specification consisted of a single in vitro assay for cytotoxicity and the following statement:

> In this test, the novel compounds, in particular the substance of Example 1, had a good action.

Ex. 44 at 3:8-9. Here, the specifications of the Patents-in-Suit disclose substantially more utility data, including numerical results expressed in terms of the IC_{50} of nucleoside analogs that inhibit HCV NS5B polymerase activity, and the EC_{50} of nucleoside analogs that inhibit HCV RNA replication. This far exceeds the statement of "a good action" that was the only test result reported in the Brana Patent.

While Gilead contends the data presented in the Patents-in-Suit support only the exemplified

compounds and not the claimed compounds, and that the presence of minor structural differences between the exemplified compounds and the claimed compounds prevents any meaningful exttrapolation, *Brana* holds otherwise. *Id*. at 1567 ("Although it is true that minor changes in chemical compounds can radically alter their effects on the human body, *Kawai*, 480 F.2d at 891, 178 USPQ at 167, evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility. *See Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 181 USPQ 453 (CCPA 1974); *Kawai*, 480 F.2d 880, 178 USPQ 158.)").

A utility disclosure that satisfies the statute does not require that claimed compounds be made or tested prior to filing a patent application; on the contrary, a specification can support the utility of compounds that have not yet been made (*actually* reduced to practice) but rather have been described in a patent application, which constitutes a *constructive* reduction to practice. *Cross*, 753 F.2d at 1044 ("Where a constructive reduction to practice is involved, as contrasted with an actual reduction to practice, a practical utility for the invention is determined by reference to, and a factual analysis of, the disclosures of the application."); *accord Atlas Powder Co. v. E.I Du Pont De Nemours & Co.*, 750 F.2d1569, 1577 (Fed. Cir. 1984) ("Use of prophetic examples . . . does not automatically make a patent no-enabling. The burden is on one challenging validity to show by clear and convincing evidence that the prophetic example together with other parts of the specification is not enabling."); *Chilowski*, 229 F.2d at 461 (rejecting the proposition that a claimed nuclear reactor "must be actually built and operated before a patent may be obtained . . . .").

The utility statement in the specification may be substantiated by submitting supporting evidence—including evidence not disclosed in the specification and evidence that is developed after filing the application in question. In *Brana*, the Federal Circuit held that even if the PTO had met its initial burden so as to shift the burden on the applicant to submit rebuttal evidence to substantiate the asserted utility, the post-filing expert declaration submitted by the applicants satisfied that requirement. 51 F.3d at 1567 ("Such evidence alone should have been sufficient to satisfy applicants' burden."). The Court explained:

> The declaration of Michael Kluge was signed and dated June 19, 1991. . . . The Kluge declaration, though dated after applicant's filing date, can be used to substantiate any doubts as to the asserted utility since this pertains

> to the accuracy of a statement already in the specification. It does not render an insufficient disclosure enabling, but instead goes to prove that the disclosure was in fact enabling when filed (i.e., demonstrated utility).

51 F.3d at 1567 n.9; *accord In re Marzocchi*, 439 F.2d at 223 n.4 (references submitted to substantiate an asserted utility need "[n]ot necessarily [be] *prior* art references . . . since the question would be regarding the *accuracy* of a statement in the specification, not whether that statement had been made before." (italics in original). "The only relevant concern of the Patent Office under these circumstances should be over the *truth* of any such assertion." *Id*. at 223.

The rule that the utility asserted in the specification may be substantiated with post-filing evidence is subject to an exception: in an interference between rival inventors, evidence of actual reduction to practice - including proof that the invention works for its intended purpose — may be needed to obtain a priority date earlier than that of a rival inventor. *See Rasmusson v. Smithline Beecham Corp*., 413 F.3d 1318, 1322, 1324 (Fed. Cir. 2005) (rejecting Rasmusson's attempt to rely on post-filing evidence of efficacy and holding that "[i]n order to obtain a priority date earlier than June 27, 1990 [the filing date accorded to SmithKline], Rasmusson needed to provide experimental proof that his invention could be effective in treating cancer."). Judge Newman explained *Rasmusson* as follows:

> The district court apparently accepted the defendant's position that such data [of utility] were required to be included in the specification. However, the purported authority cited by the defendants concerned quite different issues, where, for various reasons, it was appropriate to offer experimental evidence. For example, the district court relied on patent "interference" cases, as in *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1324 (Fed.Cir.2005), where evidence of actual reduction to practice was required to establish a priority date earlier than that of an adverse claimant.
>
> When priority is not an issue, generally the applicant may provide data obtained either before or after the patent application was filed. With reference to demonstration of utility, in *Brana*, 51 F.3d at 1567 n. 19 the court noted that post-filing evidence "can be used to substantiate any doubts as to the asserted utility since this pertains to the accuracy of a statement already in the specification."

Eli Lilly and Co. v. Actavis Elizabeth LLC, 435 Fed. Appx 917, 925 (Fed. Cir. 2011) (non-precedential)

IV. ARGUMENT

A. Inhibition of NS5B Polymerase is a Practical Utility, Disclosed in the Specification, that Supports the Asserted Claims of the '712 Patent

The '712 Patent discloses that one object of the invention is "to provide nucleoside compounds

and certain derivatives thereof which are useful as . . . inhibitors of HCV NS5B polymerase," ECF 1-2 2:51-55, and that "[t]he '5'-triphosphate derivatives of the nucleoside compounds [of the invention] are inhibitors of . . . HCV NS5B polymerase." It also substantiates this utility with data from an in vitro polymerase inhibition assay. *Id*. 138:49-50 ("Representative compounds tested in the HCV NS5B polymerase assay exhibited IC_{50}'s less than 100 micromolar").

In his expert report, Professor Mark Wentland testified: "The specifications of the '499 and '712 patents disclose that the nucleoside compounds of the invention and their derivatives are useful as inhibitors of a specific enzyme ('NS5B polymerase') of the Hepatitis C Virus . . . ." Rebuttal Expert Report of Mark Wentland, Ph.D. (Epner Decl., Ex. 56) ¶ 71.

When questioned at his deposition by Gilead's counsel, Dr. Wentland explained:

> [I]t's my opinion that the IC50 and EC values disclosed in the specification of the two patents would have provided the person of ordinary skill in the art sufficient information to understand the utility of the claimed methods and compounds.

Ex. 45 at 84:10-15.

Gilead has come forward with no evidence to contradict the above disclosure that the triphosphate compounds of the invention are useful as inhibitors of the HCV NS5B polymerase. Indeed, Gilead's expert, Dr. Seeger, **admitted** that these triphosphate compounds have that utility in the in vitro (cell free) assay, regardless of any potential toxicity in cells or animals:

> Q: So for the compounds that are described in the '712 Patent, is it necessary — is it your testimony that it is necessary to have toxicity data provided for these compounds in order for them to be useful?
>
> A Depends on what assay you are proposing to use.
>
> Q: Well, we said a cell assay but what about a cell-free assay?
>
> A: A cell-free assay is fine.
>
> Q: **So these compounds would have the utility in inhibiting the HCV virus and toxicity wouldn't matter, correct**?
>
> A: **If you are using in vitro polymerase assays, for example**.
>
> Q: **And that's a utility for these compounds**?
>
> A: **Yes**.

Ex. 46 at 126:24 – 127:19 (emphasis added). Nucleoside analogs with known inhibitory activity are now and were then extremely valuable to facilitate studying the antiviral activity of other substances under investigation, such as interferon (or other nucleoside analogs). As Dr. Seeger admitted:

> Q: And why did you correspond with—it is Dr. Schinazi, right?
>
> A: Yes. At that time, my laboratory did research on hepatitis C virus and, specifically, the interferon response against hepatitis C virus and to conduct that work **and to investigate the problems we were addressing, I needed nucleoside analogues as controls for my studies on interferon** and, for that reason, I asked Dr. Schinazi whether he could help me out.
>
> * * *
>
> Q: And did you in fact test those compounds as controls in your experiments?
>
> A: I believe we tested—I believe we used them or tested them for usefulness at that time.
>
> Q: Usefulness how?
>
> A: Just to see whether they would have an antiviral activity that we then could use to compare with our interferon work.

Ex. 46 at 14:14 – 24, 15:6 – 14 (emphasis added)[4].

The disclosed utility of inhibiting HCV NS5B polymerase is not "an inherently unbelievable undertaking or involve implausible scientific principles," *Cortright*, 165 F.3d at 1357, is not challenged by Gilead as factually inaccurate, and is supported by both sides' experts. In addition, Gilead admitted in the SOVALDI product label, in its scientific publications, and in discovery that the triphosphate metabolite of sofosbuvir (GS-461203), "**inhibited the polymerase activity of the . . . NS5B from HCV** genotype 1b, 2a, 3a and 4a . . . ." ECF 167-18 at GILEAD00000968 (emphasis added); *accord* ECF 167-17 at GILEAD00030406 ("The triphosphate metabolite [of sofosbuvir] was shown to be a potent inhibitor of HCV NS5B RNA-directed RNA polymerase."); Gilead Response to Request for Admission No. 16 (ECF 167-7) (admitting that "GS-461203 is an inhibitor of the hepatitis C virus (HCV) NS5B polymerase."). This triphosphate compound (GS-461203) infringes claims 3 and 10 of the '712 Patent. *See* ECF 167-10 ¶¶ 140-141, 216-217. It is the pharmacologically active molecule produced by

[4] Pending before the Court is Merck's motion to compel discovery concerning testing performed by Dr. Seeger for Dr. Schinazi and/or Pharmasset (ECF 161-1), which is expected to furnish additional evidence in support of validity, including utility.

sofosbuvir and its formation is essential to provide the desired pharmacological activity for treating HCV infection. *Id*. ¶ 66.

That the Accused Products, when used as directed, infringe the Asserted Claims of the '712 Patent is itself evidence that the jury is entitled to consider as supporting the utility disclosed in the '712 Patent. "It is axiomatic that one who appropriates the teachings of a patent may not deny the utility of the invention." *E.I. Du Pont de Nemours & Co. v. Berkley & Co.*, 620 F.2d 1247, 1258-59 (8th Cir. 1247) (holding that the defendant "as an infringer, was thereby estopped from asserting that [the infringed] claims are invalid for lack of utility.") (citation and internal quotation marks omitted); *Tapco Prods. Co. v. Van Mark Products Corp*., 446 F.2d 420, 428 (6th Cir. 1971) ("one who appropriates the teachings of a patent may not deny the utility of the invention"); *accord Raytheon*, 724 at 959 ("A correct finding of infringement of otherwise valid claims mandates as a matter of law a finding of utility under § 101.") (citing and following *Du Pont* and *Tapco*.) Although Gilead has elected to characterize its challenge to utility as arising under § 112 rather than § 101, these issues are "closely related," *Process Control*, 190 F.3d at 1358 , and the jury is entitled to consider Gilead's infringement as evidence of utility that refutes Gilead's challenge under § 112. *See Raytheon*, 724 F.2d at 959 ("People rarely, if ever, appropriate useless inventions."); *id*. ("The wisdom of the trial court in deciding validity and infringement, and the interrelationship of those issues, are manifested in the present case."). Evidence of infringement thus precludes summary judgment of invalidity for lack of utility.

Accordingly, the evidence shows that the '712 Patent discloses a supporting utility for the triphosphate compounds claimed in the '712 Patent, which suffices to support claims 3 and 10 of the '712 Patent. *See* ECF 167-10 ¶ 138 (claim 3 of the '712 Patent is directed to triphosphate nucleotides); *id*. ¶ 164 (same for claim 10 of the '712 Patent). Since the claimed triphosphates have utility as inhibitors of the HCV NS5B polymerase, the corresponding mono- and diphosphate compounds have utility as precursors that can be converted into those triphosphates. "Products are useful if they serve as starting materials or intermediates in producing other materials or articles which are directly useful." *Reiners v. Mehltretter*, 236 F.2d 418, 421-22 (CCPA 1956); *see also In re Fisher*, 421 F.3d 1365, 1375 (Fed. Cir. 2005); *In re Kirk*, 376 F.2d 936, 946 (CCPA 1967). Accordingly, the disclosed utility of inhibiting HCV NS5B polymerase also supports claims 1 and 5 (directed to monophosphate compounds;

see ECF 167-10 ¶¶126, 144), claims 2, 7 and 11 (directed to diphosphate compounds; *see id.* ¶¶ 132, 150, 170), and claim 9 of the '712 Patent (directed to di-and triphosphate compounds; *see id.* ¶ 156).

Thus, a reasonable jury could find that Gilead has not met its burden to prove by clear and convincing evidence that the '712 Patent specification fails to disclose a practical utility for the compounds claimed in the Asserted Claims of the '712 Patent, namely: inhibition of HCV NS5B polymerase. This ground in and of itself requires denial of summary judgment with respect to the Asserted Claims of the '712 Patent.

B. Treatment of HCV Infection is a Practical Utility, Disclosed in the Specifications of the Patents-In-Suit, that Supports the Asserted Claims of the '712 and '499 Patents

The '499 and '712 Patents disclose that one object of the invention is "to provide nucleoside compounds and certain derivatives which are useful . . . in the treatment of HCV infection," ECF 1-1 2:50-53; ECF 1-2 2:60-63, and that "[t]he instant nucleoside compounds and derivatives thereof are useful to treat . . . HCV infection." ECF 1-1 2:38-40; ECF 1-2 2:48-50. The Patents-in-Suit also provide supporting data from two assays to substantiate this asserted utility. ECF 1-1 132:56-57; ECF 1-2 138:49-50 ("Representative compounds tested in the HCV NS5B polymerase assay exhibited IC_{50}'s less than 100 micromolar."); ECF 1-1 133:22-23; ECF 1-2 139:15-16 ("Representative compounds tested in the replication assay exhibited EC_{50}'s less than 100 micromolar.").

Professor Wentland testified in his expert report: "The specifications of the '499 and '712 patents disclose that the nucleoside compounds of the invention and their derivatives are useful as . . . agents for treating HCV infections." Ex. 56 ¶ 71; *see also* Ex. 45 at 84:11-15 (testifying that "the IC50 and EC values disclosed in the specification of the two patents would have provided the person of ordinary skill in the art sufficient information to understand the utility of the claimed methods and compounds.").

The disclosed utility of treating HCV infection does not "suggest an inherently unbelievable undertaking or involve implausible scientific principles," *Cortright*, 165 F.3d at 1357. On the contrary, there was ample precedent, as of the January 18, 2002 filing date, for therapeutic use of nucleoside analogs to treat viral infections. Such agents were recognized as "the cornerstone of antiviral therapy over the [prior] 30 years." Ex. 6 at 9. By January 2002, the FDA had approved no fewer than seventeen (17) nucleoside analogs for the treatment of nine (9) viral infections, including HCV. Exs. 7 to 43.

Accordingly, there was no "reason to doubt the objective truth of the statements contained in the written description," *Cortright*, 165 F.3d at 1357, and the applicants were under no duty to provide evidence to substantiate the utilities asserted in the specification, which were entitled to be considered "presumptively correct." *Brana*, 51 F.3d at 1566.

Even so, the specifications of the '499 and '712 Patents ***did*** disclose evidence to establish that the claimed compounds possess the asserted utility. The claimed compounds are structurally similar to compounds that are exemplified in the specification, which themselves are supported by data from the NS5B polymerase assay and the HCV RNA replication assay (HCV "replicon" assay) in that they share the "key structural features related to their use in treating . . . HCV infection" by virtue of "a selective ability to inhibit RNA viral polymerases, and in particular the HCV NS5B polymerase." Ex. 51 ¶¶ 110, 146. A reasonable jury is entitled to credit Dr. Wuest's testimony and to find that the claimed compounds have utility. *Brana*, 51 F.3d at 1567 ("Although it is true that minor changes in chemical compounds can radically alter their effects on the human body, evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility.").

The Patents-in-Suit also provide the underlying rationale that explains, in accordance with sound scientific principles, how the compounds of the invention work to treat HCV infection:

> Inhibition of HCV NS5B polymerase prevents formation of the double-stranded HCV RNA and therefore constitutes an attractive approach to the development of HCV-specific antiviral therapies.

ECF 1-1 2:28-31; ECF 1-2 2:38-41. Carroll et al. "provided a large body of data in support of their claims." Ex. 51 ¶ 75. "A person of ordinary skill in the would have recognized that the [HCV] replicon assay is particularly informative because observation of an inhibitory effect provides evidence that the tested compound is both a substrate for triphosphorylation and an inhibitor of RNA replication under the relevant cellular conditions." *Id.* ¶ 97. Gilead's expert, Dr. Seeger, has acknowledged that the HCV replicon assay was accepted to screen and identify compounds for anti-HCV activity. Testifying as Gilead's expert in a Canadian litigation where Gilead was challenging the validity of a patent owned by Idenix (Merck's subsidiary) because it allegedly did **not** provide data from the HCV replicon assay, Dr. Seeger opined as follows:

> The HCV replicon assay was rapidly adopted by the leaders in the anti-

> HCV field for evaluating select potential anti-HCV compounds with a view toward developing drugs for treating HCV infection in humans.

Ex. 47 ¶ 67.

A reasonable jury is entitled to credit Dr. Seeger's testimony in the Canadian litigation that the HCV replicon assay is an appropriate assay for screening and identifying compounds for utility in treating HCV infection. This is more than sufficient to substantiate the asserted therapeutic utility. "The stage at which an invention in this field [of pharmaceutical inventions] becomes useful is well before it is ready to be administered to a human." *Brana*, 51 F.3d at 1568; *id* at 1567 (criticizing the PTO for "confus[ing] the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption").

Accordingly, a reasonable jury is entitled to conclude that the asserted utility of treating HCV infection is supported by the fact that the inventors of the Patents-in-Suit used this same HCV replicon assay in the Structure Activity Relationship analysis that led them to conceive and describe the classes of compounds that are claimed in the '712 Patent, and whose administration to treat HCV infection is claimed in the '499 Patent.

Moreover, Pharmasset's real-world use of the Merck '499 Publication to guide its HCV nucleoside research in 2002 and thereafter, described above, provides strong evidence that a person of ordinary skill in the art would have perceived a practical utility disclosed in the Merck '499 Publication upon reading it in January 2002. A reasonable jury is entitled to conclude from this evidence that the utility assertion in the Patents-in-Suit was credible in January 2002.

In addition, Gilead has admitted that use of the Accused Products, in accordance with their respective labels results in use of (a) the methods defined by the Asserted Claims of the '499 Patent and (b) the compounds defined by the Asserted Claims of the '712 Patent. ECF 154 at 2. If the jury finds (or the Court grants summary judgment) that one or more of the Asserted Claims is infringed by Gilead's Accused Products, that alone would support a jury finding that the infringed claims have utility. *Raytheon*, 724 F.2d at 959; *Du Pont*, 620 F.2d at 1258-59, *Tapco*, 446 F.2d at 428. The evidence of infringement thus precludes summary judgment of invalidity.

C. Gilead's Motion Misstates the Law and the Facts

In the face of abundant evidence of utility, Gilead seeks refuge in a smokescreen of unfounded

allegations calculated to foster the false impression that Merck derived the invention at issue in this litigation from Pharmasset, Gilead's subsidiary. Precisely the opposite is true. The evidence shows that Dr. Carroll et al. (Merck's inventors) were first, and that they filed patent applications describing the invention set forth in the Asserted Claims of the Patents-in-Suit on January 18, 2002—almost a year before Jeremy Clark at Pharmasset thought of making PSI-6130 (the compound that features so prominently in Gilead's fanciful account). In fact, it was Pharmasset that stood on Merck's shoulders. The evidence shows that Pharmasset scientists read and copied from the disclosure of the '499 Patent, which was published as a PCT Application on July 25, 2002. Pharmasset scientists were fully aware of Merck's prior invention when they turned to sofosbuvir as a means for delivering Merck's claimed compounds to the cells of the liver in order to treat HCV infection. Gilead complains that Merck—allegedly—amended its claims during prosecution of the '499 Patent to ensure that they covered the use of PSI-6130.[5] Even if that allegation were true, it is simply irrelevant, as a matter of law, to the validity of the Patents-in-Suit:

> [N]or is it in any manner improper to amend or insert claims intended to cover a competitor's product the patent applicant's attorney has learned about during the prosecution of a patent application. Any such amendment or insertion must comply with all statutes and regulations, of course, but, if it does, its genesis in the marketplace is simply irrelevant and cannot of itself evidence deceitful intent.

Kingsdown Med. Consultants v. Hollister Inc., 863 F.2d 867, 874 (Fed. Cir. 1988).

Gilead's challenge to the utility of the '499 and '712 Patents is fundamentally flawed, as shown by its inappropriate reliance on factually inapposite cases. *In Re '318 Patent Infringement Litigation*, 583 F.3d 1317 (Fed. Cir. 2009) is inapplicable here. That case concerned a patent whose specification was "only just over one page in length," directed to a new use for a prior art compound called "galanthamine": treating Alzheimer's disease. *Id*. at 1321; *see* U.S. Patent No. 4,663,318 (Ex. 48). The specification provided "neither in vitro test results nor animal results involving the use of galantamine to treat Alzheimer's disease," *In re '318 Patent*, 583 F.3d at 1325, and identified several prior art references that tested galantamine for other indications, which were asserted at trial as grounds for obviousness. *Id*.

[5] The claim amendments that Gilead complains of occurred after Pharmasset published the structure of PSI-6130.

The patentee overcame the obviousness challenge by persuading the trial court that the prior art uses "did not establish galantamine's utility in treating Alzheimer's disease." *Id*. at 1325-26. Under these circumstances, the Court did not permit the patentee to rely on those same prior art references as supporting the claimed methods by "analytic reasoning" in the absence of data. *Id*. at 1326. The Court also precluded the patentee from relying on post-filing test results, distinguishing *Brana* on the grounds that the specification in that case did include "in vitro test results" in support of utility. *Id*. at 1325 & n.8. The patent at issue in that case has nothing in common with the Patents-in-Suit, which describe the "major" scientific endeavor undertaken by the inventors and provide data far in excess of the statement of "a good action" in the *Brana* patent.

Nor does the decision in *CreAgri, Inc. v Pinnaclife, Inc.*, No. 11-CV-6635-LHK, 2013 WL 6673676, (N.D. Cal. Dec. 18, 2013), *aff'd* 579 Fed. App'x 1003 (Fed. Cir. 2014), support Gilead. In *CreAgri*, the court reasoned that utility is established where either (a) one of skill in the art would accept the utility statement without question, or (b) the specification contains "some quantum of data or reasoning" that supports the utility statement. *Id*. at *17. The "uncontroverted" expert evidence showed that the class of compound in question ("olive-oil derived polyphenols") had no established therapeutic effect at the relevant filing date. *Id*. at *17-18. The court rejected the patentee's reliance on post-filing evidence because the patent at bar made "no assertions whatsoever about the outcomes of the studies proposed in the specification" so that the later results "did not pertain to the accuracy of a statement in the specification within the meaning of *Brana*." *Id*. at *19. And even if considered, those references did not support the asserted claims. *Id*. Moreover, the specification was devoid of "argument or analytic reasoning" in support of the asserted utility. *Id*. at *20-21. The facts of *CreAgri* are entirely distinguishable. The Patents-in-Suit provide both data and scientific rationale in support of the asserted utility, which (a) satisfies the utility requirement without reliance on post-filing data, and (b) justifies reliance on post-filing evidence to substantiate the accuracy of the utility assertion in the specification. Moreover, the evidence shows that nucleoside compounds were well accepted as antiviral agents by January 2002.

D. Gilead's Motion for Summary Judgment of Invalidity Should Be Rejected on Multiple Grounds.

First, the assertion of utility in the specifications of the '499 and '712 is not "inherently unbelievable" and does not involve "implausible scientific principles." *Cortwright*, 165 F.3d at 1357. On the contrary, nucleoside analogs were well known as the "cornerstone" of antiviral therapy, as demonstrated by FDA approval of numerous nucleoside analogs as agents for treatment of viral infections including HCV. Accordingly, the utility disclosure in the Patent-in-Suit did not require corroboration and "*must* be taken as in compliance with the enabling requirement of §112." *Brana*, 51 F.3d at 1566. This alone justifies denial of Gilead's Motion.

Second, Gilead has offered no evidence to gainsay the usefulness of the compounds of the '712 Patent to inhibit the HCV NS5B polymerase in a cell-free assay. It is undisputed that inhibitors of HCV NS5B polymerase have utility, as Gilead's own expert admitted. This alone requires that Gilead's Motion be denied with respect to the '712 Patent.

Third, to the extent that the utilities asserted in the Patents-in-Suit require corroboration, the specifications provide ample data, as explained by Professors Wuest and Wentland, including the results of the NS5B polymerase assay and the RNA replication assay. Gilead's reliance on *Petito v. Puritan's Pride, Inc.*, 35 F. Supp. 3d 494 (S.D.N.Y. 2014) for the proposition that the Patents-in-Suit do not include "data" is misplaced. In *Petito*, unlike this case, the asserted utility was "not supported by experimental results—whether human, animal, or in vitro." *Id*. at 508. During prosecution the applicants had submitted the "Polen letter" to the examiner recounting testimonials from users said to have benefited from the invention, s*ee id*. at 498-99, but the patentees did not attempt to rely on that letter in support of utility. *Id*. at 508. The patent in *Petito* fails to identify any tests that were performed with the claimed compositions and contains no disclosure of any test results whatsoever. *See* U.S. Patent No. 6,645,948 (Ex. 49). Under these circumstances, the *Petito* court rejected the patentees' argument that the bare identification of the "therapeutic effects" alleged to flow from using the claimed compositions constituted "data" in support of utility. 35 F. Supp. 3d at 508. The patent in *Petito* bears no resemblance whatsoever to the Patents-in-Suit, which describe a major scientific endeavor and disclose the numerical IC_{50} and EC_{50} results achieved in two assays of efficacy, including the "HCV replicon" assay that,

Gilead's own expert admitted, was "adopted by leaders in the anti-HCV field for evaluating select anti-HCV compounds" as antiviral therapeutics. *See* Ex. 47 ¶¶ 67, 70. The data disclosed in the 'Patents-in-Suit far exceed the statement of "a good action" that constituted the only utility test result in the Brana specification, which has been acknowledged as constituting "in vitro test results" in support of utility. *In Re '318 Patent*, 583 F.3d at 1325 n.8. This is an independent ground for denying Gilead's Motion.

Fourth, a jury finding (or summary judgment) of infringement would independently support a finding that the infringed claim(s) have utility. Given the Joint Stipulation and other infringement evidence submitted with Merck's pending summary judgment motion (ECF 167), this is an additional ground for denying Gilead's Motion.

Fifth, the scientific data concerning sofosbuvir's mode of action provides additional evidence of utility of the Patents-in-Suit. As shown by the testimony of Professor Benet, sofosbuvir works by converting, successively, into mono-, di-, and triphosphate compounds that are patented (and whose use is patented) by Merck which results in (a) inhibiting the HCV NS5B polymerase and (b) treating HCV infection—exactly as disclosed in the specifications of the '499 and '712 Patents. The mode of action of sofosbuvir, and its commercial success, provides additional grounds for denying Gilead's Motion. It is undisputed that Gilead has sold [redacted] dollars of its accused sofosbuvir products since 2013. It is further undisputed that, at the time Gilead launched its sofosbuvir products, its internal projections stated that they would be sold at more than a [redacted]% gross margin. Ex. 54, Ex. 55 at GILEAD02412754, Ex. 57. "Proof of . . . utility is further supported when, as here, the inventions . . . have on their merits been met with commercial success." *Raytheon*, 724 F.2d at 959.

V. CONCLUSION

For the reasons set forth above, a reasonable jury is entitled to conclude that the specification of the '499 and '712 Patents discloses at least one practical utility that supports each of the Asserted Claims. Accordingly, Merck respectfully requests that this Court deny Gilead's Motion in its entirety.

Dated: November 12, 2015

STEPHEN S. RABINOWITZ
JAMES W. DABNEY
PATRICE P. JEAN
WANDA D. FRENCH-BROWN
MITCHELL EPNER
DAVID E. LANSKY
HUGHES HUBBARD & REED LLP

RANDY C. EISENSMITH
NAZ E. WEHRLI
FRIED, FRANK, HARRIS, SHRIVER & JACOBSON LLP

JOSHUA H. LERNER
LAURA E. MILLER
DURIE TANGRI LLP

By: */s/ Stephen S. Rabinowitz*
STEPHEN S. RABINOWITZ

Attorneys for Defendant MERCK & CO., INC. and Defendants and Counterclaimants MERCK SHARP & DOHME CORP. and ISIS PHARMACEUTICALS, INC.

CERTIFICATE OF SERVICE

I certify that all counsel of record are being served on November 12, 2015 with a copy of this document via the Court's CM/ECF system.

/s/ Stephen S. Rabinowitz
STEPHEN S. RABINOWITZ